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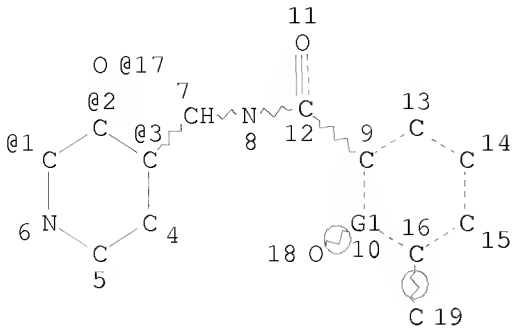

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STEREO ATTRIBUTES: NONE

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FULL SEARCH INITIATED 15:09:20 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 595 TO ITERATE

100.0% PROCESSED 595 ITERATIONS 153 ANSWERS
SEARCH TIME: 00.00.01

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=> fil caplus
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	181.12	181.33

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FILE LAST UPDATED: 8 Oct 2008 (20081008/ED)

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http://www.cas.org/legal/infopolicy.html

=> s l3
L4 6 L3

=> d bib abs 1-6

L4 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:523944 CAPLUS
DN 145:76502
TI Differential effects of 5-hydroxytryptamine4 receptor agonists at gastric versus cardiac receptors: an operational framework to explain and quantify organ-specific behavior
AU De Maeyer, Joris H.; Prins, Nicolaas H.; Schuurkes, Jan A. J.; Lefebvre, Romain A.
CS Heymans Institute of Pharmacology, Ghent University, Ghent, Belg.
SO Journal of Pharmacology and Experimental Therapeutics (2006), 317(3), 955-964
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Quantification of different levels of 5-hydroxytryptamine4 (5-HT4) receptor agonism expression across animal species as well as across organs within the same animal species offers substantial potential for the separation of desired gastrointestinal vs. undesired cardiac pharmacol. activity of compds. in development. Since a detailed investigation of such properties is lacking to date, we set out to quantify gastric and cardiac effects of 5-HT4 receptor ligands in the pig, a model considered to be representative for the human situation. An in vitro test was developed to study the potentiating effect of 5-HT, prucalopride, tegaserod, R149402 (4-amino-5-chloro-2,2-dimethyl-2,3-dihydro-benzofuran-7-carboxylic acid [3-hydroxy-1-(3-methoxy-propyl)-piperidin-4-ylmethyl]-amide), and R199715 (4-amino-5-chloro-2,3-dihydro-benzofuran-7-carboxylic acid [3-hydroxy-1-(3-methoxy-propyl)-piperidin-4-ylmethyl]-amide) on elec. induced cholinergic contractions in longitudinal muscle strips of the proximal stomach. The results were compared with inotropic and chronotropic effects of these compds. in the elec. paced left atrium and spontaneously beating right atrium, resp. To quantify the observed tissue-dependent responses, a nonlinear mixed-effects model based on the operational model of agonism was developed and successfully fitted to the data. The model quantified the tissue-dependent partial agonism of the selective 5-HT4 receptor agonists prucalopride, R149402, and R199715, whereas tegaserod and 5-HT were equiefficacious. The model was further extended to incorporate the responses to prucalopride in the presence of the 5-HT4 receptor antagonist GR113808 ([1-[2-[(methylsulfonyl)amino]ethyl]-4-piperidinyl]methyl 1-methyl-1H-indole-3-carboxylate). The results indicate that these interactions do not follow a simple competitive pattern and that they differ between stomach and left atrium.
RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2006:63851 CAPLUS
DN 144:362812
TI Porcine left atrial and sinoatrial 5-HT4 receptor-induced responses: fading of the response and influence of development
AU De Maeyer, Joris H.; Straetemans, Roel; Schuurkes, Jan A. J.; Lefebvre, Romain A.
CS Heymans Institute of Pharmacology, Ghent University, Ghent, Belg.
SO British Journal of Pharmacology (2006), 147(2), 140-157
CODEN: BJPCBM; ISSN: 0007-1188
PB Nature Publishing Group
DT Journal
LA English
AB In this study, we aimed to characterize in vitro the effects of the benzofuran 5-HT4 receptor agonists prucalopride, R149402 and R199715 and the indolic agents tegaserod and 5-HT in the atria of young pigs (10-11 wk) and newborn piglets. In the paced left atrium of young pigs, only 5-HT results in pos. inotropic responses when administered cumulatively (maximal effect relative to isoprenaline=53%, pEC50=6.8); however, all agonists showed lusitropic effects. Noncumulative administration results in greater pos. inotropic responses for 5-HT and induces moderate pos. inotropic responses for the other agonists; these responses fade. Phosphodiesterase (PDE) enzyme inhibition with 3-isobutyl-1-methylxanthine (IBMX; 20 μM) enhances the responses to cumulatively administered 5-HT (maximal effect=89%, pEC50=7.7) and reveals clear pos. inotropic effects for prucalopride, tegaserod, R149402 and R199715; fading is abolished. The maximal effect of the benzofurans is less pronounced than that of the indoles. In the spontaneously beating right atrium of young pigs, all agonists show chronotropic activity when administered cumulatively in the absence of IBMX, without fade. Benzofurans behaved as partial agonists compared to 5-HT (maximal effect=54%, pEC50=6.5). In newborns, the inotropic activity of the agonists in the IBMX-treated left atrium was less pronounced than in the young pig; the same applied for the chronotropic response in the right atrium, except for 5-HT. In conclusion, the atrial responses to 5-HT4 receptor activation increase in the first months of life; the inotropic response is regulated by PDEs. Prucalopride, R149402 and R199715 are partial agonists compared to 5-HT.
RE.CNT 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2004:663739 CAPLUS
DN 141:355497
TI Fast method development and rapid analysis using a screening approach for enantiomeric separations in capillary electrophoresis
AU Jimidar, M. Ilias; van Ael, Willy; Shah, Rekha; Redlich, Dirk; de Smet, Maurits
CS Johnson and Johnson Pharmaceutical Research and Development, Global Analytical Development, Janssen Pharmaceutica N.V., Beerse, Belg.
SO Journal of Capillary Electrophoresis and Microchip Technology (2003), 8(5/6), 101-110
CODEN: JCEMF6
PB ISC Technical Publications, Inc.
DT Journal
LA English
AB To speed up the trial-and-error process during enantioselective capillary electrophoresis methods development, a systemized approach is proposed to develop methods by applying several screening methods in the search for an initial separation Screening methods combine high selectivity with broad applicability and are applied to find an initial enantiomeric separation during early pharmaceutical development (pre-Phase 1 to Phase 1). The goal is to

achieve enantiomeric separation rapidly to characterize the chiral purity of pharmaceutical products. Dedicated, highly efficient screening methods are suggested for basic, neutral, and acidic compds. In these screening methods, multiple chiral selectors are applied in mixts. at different buffer pH values. For the compds. studied, the technique allows fast method development. Furthermore, it is potentially applicable to a wide range of low-mol.-weight compds. and permits rapid anal. at low cost, since runs are performed in inexpensive, bare silica capillaries using ordinary buffer systems with only typical cyclodextrins as the selector. Along with simplicity and robustness, the approach results in sufficient efficacy (i.e., it is easy, straightforward, and reproducible, with a high success rate). Typical pharmaceutical applications are described. The major advantage of the screening approach to methods development is the decrease in development cycle time. The total screening time for 1 compound was about 5.3 h on 1 CE instrument.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2002:408547 CAPLUS
DN 136:395967
TI Use of a triple combination comprising a 5-HT3 antagonist, a 5-HT4 agonist, and a laxative for promoting intestinal lavage and treating constipation
IN Megens, Antonius Adrianus Hendrikus Petrus
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002041918	A2	20020530	WO 2001-EP13318	20011115
	WO 2002041918	A3	20020711		
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	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2428386	A1	20020530	CA 2001-2428386	20011115
	AU 2002031627	A5	20020603	AU 2002-31627	20011115
	EP 1347779	A2	20031001	EP 2001-991729	20011115
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004513969	T	20040513	JP 2002-544095	20011115
	US 20040096423	A1	20040520	US 2003-432811	20031224
PRAI	EP 2000-204191	A	20001124		
	WO 2001-EP13318	W	20011115		

AB The invention discloses the use of a triple combination comprising a 5-HT3 antagonist, a 5-HT4 agonist and a laxative, in particular an osmotic agent, for accelerating intestinal lavage. The invention also discloses the use of the above triple combination for the treatment of constipation.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 2000:441788 CAPLUS
DN 133:74035

TI Preparation of 4-(aminomethyl)piperidinebenzamides as gastrointestinal agents.

IN Bosmans, Jean-Paul Rene Marie Andre; Meulemans, Ann Louise Gabrielle; De Cleyn, Michel Anna Jozef; Gijsen, Henricus Jacobus Maria

PA Janssen Pharmaceutica N.V., Belg.

SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037461	A1	20000629	WO 1999-EP10064	19991214
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	TW 570920	B	20040111	TW 1999-88121125	19991203
	CA 2355857	A1	20000629	CA 1999-2355857	19991214
	BR 9916491	A	20010904	BR 1999-16491	19991214
	EP 1140915	A1	20011010	EP 1999-967956	19991214
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	TR 200101962	T2	20020422	TR 2001-1962	19991214
	HU 2001004838	A2	20020729	HU 2001-4838	19991214
	HU 2001004838	A3	20030528		
	EE 200100335	A	20020815	EE 2001-335	19991214
	JP 2002533337	T	20021008	JP 2000-589532	19991214
	NZ 512871	A	20021126	NZ 1999-512871	19991214
	AU 770397	B2	20040219	AU 2000-24328	19991214
	IL 143858	A	20050320	IL 1999-143858	19991214
	AT 297917	T	20050715	AT 1999-967956	19991214
	PT 1140915	T	20051130	PT 1999-967956	19991214
	ES 2245131	T3	20051216	ES 1999-967956	19991214
	SK 285829	B6	20070906	SK 2001-859	19991214
	PL 197409	B1	20080331	PL 1999-348417	19991214
	IN 2001MN00442	A	20050304	IN 2001-MN442	20010423
	BG 105571	A	20020131	BG 2001-105571	20010607
	BG 64953	B1	20061031		
	NO 2001002858	A	20010608	NO 2001-2858	20010608
	NO 321324	B1	20060424		
	US 6544997	B1	20030408	US 2001-857905	20010608
	HR 2001000445	A1	20020630	HR 2001-445	20010614
	MX 2001PA06409	A	20010910	MX 2001-PA6409	20010621
	ZA 2001005135	A	20020621	ZA 2001-5135	20010621
	HK 1039114	A1	20050819	HK 2002-100161	20020129
	US 20030181456	A1	20030925	US 2003-353307	20030129
	US 7205410	B2	20070417		
PRAI	EP 1998-204411	A	19981222		
	WO 1999-EP10064	W	19991214		
	US 2001-857905	A3	20010608		

OS MARPAT 133:74035

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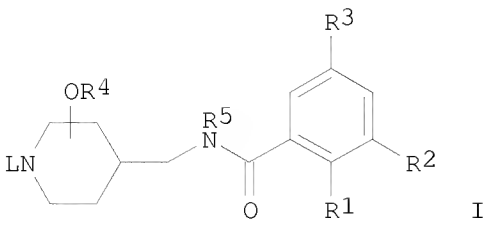

I

AB Title compds. [I; R1R2 = (substituted) OCH2O, OCH2CH2, OCH2CH2O, etc.; R3 = H, halo; R4, R5 = H, alkyl; L = cycloalkyl, oxocycloalkyl, alkenyl, etc.], were prepared Thus, trans-N-[1-(3-aminopropyl)-3-hydroxy-4-piperidinyl]methyl-7-chloro-2,3-dihydro-1,4-benzodioxin-5-carboxamide (preparation given). Was stirred with 2-chloro-3-methylpyrazine and CaO at 120° to give 16% trans-7-chloro-2,3-dihydro-N-[[3-hydroxy-1-[3-[(3-methyl-2-pyrazinyl)amino]propyl]-4-piperidinyl]methyl]-1,4-benzodioxin-5-carboxamide. This antagonized 5HT4 in rat esophageal tunica muscularis mucosae with pA2 = 10.55.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2008 ACS on STN
AN 1999:64684 CAPLUS
DN 130:139258
TI Gastrokinetic bicyclic benzamides of 3- or 4-substituted 4-(aminomethyl)piperidine derivatives
IN Bosmans, Jean-Paul Rene Marie Andre; De Cleyn, Michel Anna Jozef; Surkyn, Michel
PA Janssen Pharmaceutica N.V., Belg.
SO PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9902156	A1	19990121	WO 1998-EP4190	19980707
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IN 189031	A1	20021207	IN 1998-DE1609	19980611
TW 402591	B	20000821	TW 1998-87109332	19980612
TW 548103	B	20030821	TW 1998-87109331	19980612
CA 2295088	A1	19990121	CA 1998-2295088	19980707
CA 2295088	C	20071023		
AU 9888574	A	19990208	AU 1998-88574	19980707
AU 734475	B2	20010614		
EP 991410	A1	20000412	EP 1998-940158	19980707
EP 991410	B1	20021030		
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TR 200000022	T2	20000621	TR 2000-22	19980707
TR 200000023	T2	20000921	TR 2000-23	19980707
BR 9811688	A	20000926	BR 1998-11688	19980707

	EE 200000015	A	20001016	EE 2000-15	19980707
	EE 4178	B1	20031215		
	HU 2000002539	A2	20001228	HU 2000-2539	19980707
	HU 2000002539	A3	20020328		
	NZ 502209	A	20010126	NZ 1998-502209	19980707
	JP 2002508000	T	20020312	JP 1999-508125	19980707
	EP 1206938	A1	20020522	EP 2002-75710	19980707
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	AT 226820	T	20021115	AT 1998-940158	19980707
	PT 991410	T	20030331	PT 1998-940158	19980707
	ES 2187051	T3	20030516	ES 1998-940158	19980707
	CN 1117568	C	20030813	CN 1998-806950	19980707
	IL 133918	A	20040620	IL 1998-133918	19980707
	ES 2212330	T3	20040716	ES 1998-939620	19980707
	CZ 295506	B6	20050817	CZ 1999-4587	19980707
	PL 190611	B1	20051230	PL 1998-338008	19980707
	SK 284942	B6	20060202	SK 1999-1840	19980707
	CZ 297298	B6	20061115	CZ 1999-4638	19980707
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	ZA 9806167	A	20000110	ZA 1998-6167	19980710
	BG 63709	B1	20021031	BG 1999-103983	19991210
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	US 6635643	B2	20031021		
	IN 194706	A1	20041127	IN 2002-DE188	20020301
	IN 2002DE00187	A	20050311	IN 2002-DE187	20020301
	US 20040058958	A1	20040325	US 2003-643506	20030819
	US 20060142341	A1	20060629	US 2006-355326	20060216
	US 20060142342	A1	20060629	US 2006-357884	20060217
	US 20070037850	A1	20070215	US 2006-584732	20061020
PRAI	EP 1997-202180	A	19970711		
	EP 1998-200624	A	19980227		
	IN 1998-DE1609	A3	19980611		
	EP 1998-940158	A3	19980707		
	WO 1998-EP4190	W	19980707		
	US 1998-113635	B1	19980710		
	US 1999-349912	B1	19990708		
	US 2001-791227	A3	20010222		
	US 2003-643506	B1	20030819		
	US 2006-357884	B1	20060217		

OS MARPAT 130:139258

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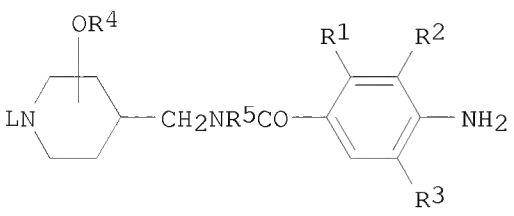

I

AB The title compds. [R1R2 = a bivalent radical; R3 = H, halo; R4 = H, C1-6alkyl; R5 = H, C1-6alkyl; L = C3-6cycloalkyl, C5-6cycloalkanone, C2-6alkenyl, etc.], useful for treating conditions which are related to impairment of gastric emptying, were prepared E.g., trans-5-amino-N-[[1-(2-aminoethyl)-3-hydroxy-4-piperidinyl]methyl]-6-chloro-3,4-dihydro-2H-1-benzopyran-8-carboxamide was prepared The effects of I on gastric emptying of an acaloric liquid meal was investigated in dogs.

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT